

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	The impact of various neurological disorders on the risk for falls in the community dwelling elderly: a case controlled study
AUTHORS	Homann, Carl; Homann, Barbara; Plaschg, Annemarie; Grundner, Marion; Haubenhofner, Alice; Griedl, Theresa; Ivanic, Gerd; Hofer, Edith; Fazekas, Franz

VERSION 1 - REVIEW

REVIEWER	Professor Zvezdan Pirtošek, MD, PhD Head of Department of Neurology, UMC Ljubljana, Slovenia No conflict of interests.
REVIEW RETURNED	01-Jul-2013

GENERAL COMMENTS	This simple but nice study - first of the kind, providing comparison between several neurological diseases of elderly ambulatory neurological patients - offers an important message for a general practitioner, geriatrician, neurologist and carer: patients with even only mild to moderate neurological affection are two to three times more likely to fall. Not only those with clear affection of sensori-motor & gait & balance systems, but also in those diagnosed with affections not related directly to these systems.
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REVIEWER	Peter Overstall Locum consultant in geriatric medicine Powys Teaching Local Health Board UK I have no competing interests.
REVIEW RETURNED	27-Jul-2013

THE STUDY	Consensus guidelines recommend the use of prospective falls diaries in studies on fall rates, eg monthly diaries returned to the researcher who can telephone patients to remind them if necessary. The absence of diaries is a serious flaw and means the fall rates are likely to be underestimated. Also it is not stated whether patients were given a simple definition of a fall and again this is necessary to ensure accuracy. For instance, was a fall during an epileptic fit counted as a fall?
GENERAL COMMENTS	I imagine that many of these patients would have a fear of falling and this would be an interesting area to include if you are planning further studies. The effect of medication on balance in this group of patients would also be worth looking at. I entirely agree with your message that neurological patients should be regarded as having a high falls risk. Well done!

REVIEWER	Colleen G Canning The University of Sydney I have no conflicts of interest.
REVIEW RETURNED	02-Sep-2013

THE STUDY	<p>Title Suggest remove “various” from the title</p> <p>Is the research question clearly defined? Yes, however, there is already a substantial amount known about increased risk of falls in the stroke and Parkinson’s disease population and it is recommended that this be acknowledged (eg, Verheyden G, 2013, Cochrane Database of Systematic Reviews 10; CD008728; Allen NE, 2013, Parkinson’s disease 2013:906274). The potential new information relates to the cumulative effect of more than one neurological condition (and other conditions) and the risk of falls in yet unstudied populations, eg, such as headache.</p> <p>Is the overall study design appropriate and adequate to answer the research question? As a preliminary investigation, yes. Future studies using gold standard prospective falls monitoring are required with larger sample sizes for neurological subgroups are required in order to confirm observations</p> <p>Are the participants adequately described, their conditions defined, and the inclusion and exclusion criteria described? Inclusion and exclusion criteria are not clearly described. A small number of participants were included with dementia. What specific criteria were used to exclude on the basis of cognitive impairment? The control participants were required to be without other disabling medical conditions – could the authors please provide examples of conditions that were in this category. It is not clear that other disabling medical conditions were also excluded in those with neurological conditions? It is not clear if the control participants were screened for cognitive impairment?</p> <p>Are the patients representative of actual patients the evidence might affect? It is not clear how many participants were invited to participate at the time of the neurological examination, how many declined and for what reasons. The Barthel index data presented in Table 2 suggests that those included were a relatively high-functioning group.</p> <p>Are the methods adequately described? The paragraph titled “Epidemiological and environmental bases” could contain less detail. Please explain how the 13 categories of neurological conditions were determined? For example, is this a standard classification reported in the literature? It is not clear which measures were taken at the baseline assessment performed by CNH and which measures were collected in the telephone questionnaire? For example, the motor examination of the UPDRS and the Hoehn & Yahr scale requires observation by the examiner, but it appears these data were collected in the telephone interview? Also, these data don’t appear to be reported in the results.</p>
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	<p>The ABC-6 scale does not appear to have administered according to the guidelines. In these guidelines participants are asked to “indicate your level of confidence in doing the activity without loss of balance or being unsteady”? (Powell and Meyers, Journals of Gerontology 1995;50A:M28-M34) which is different to being asked about confidence in doing the activity without falling. A more appropriate heading for this section would be simply “Balance Confidence”. I would also suggest that “analysis of” be removed from the other headings in this section.</p> <p>Please provide the “predefined algorithm” mentioned on line 42, page 7. The rationale for identifying “matched pairs” of participants with a neurological condition and control is not clear, especially given that other than results presented in Table 1, all statistical analyses relate to the larger cohorts (228 neurological outpatients and 193 healthy controls).</p> <p>Is the main outcome measure clear? Please state explicitly that the primary outcomes was falls, based on participant recall over the prior 12 months. Please explain how a fall was defined and provide a reference for the definition?</p> <p>Are the abstract/summary/key messages/limitations accurate? The abstract should state explicitly that falls data was based on 12 month recall of falls. The percentages should be identified as proportion of fallers in each subgroup, not fall frequency. Article summary – there is more than limited falls data on some neurological impairments, eg, PD and stroke, and most of this data relates to community dwelling persons Key messages - The new information relates to the cumulative effect of more than one neurological condition (and other conditions) and the risk of falls in yet unstudied populations, eg, such as headache. This could be made clearer. Suggest remove “astonishingly” Strengths and limitations – although the design is prospective, the falls history is retrospective, based on recall over 12 mths. Are the statistical methods described?</p> <p>Are they appropriate? It is reported that risk odds ratios were computed – please clarify whether these are odds ratios or risk ratios? The results should be amended in line with this. Is the standard of written English acceptable for publication? English language editing would improve clarity Are references up to date and relevant? Ref 2 – this Cochrane review was updated in 2012 (Gillespie LD, 2012, Cochrane Database of Systematic Reviews 9;CD007146) Ref 11 – this is a retrospective study of falls in people with PD. There are several high quality prospective studies, which would be more appropriately referenced, eg, Latt MD, 2009, Movement Disorders 24:1280-9; Kerr GK, 2010, Neurology 75:116-24; Paul SS, 2013, Movement Disorders 28:655-62. See also comments relating to discussion Do any supplemental documents, eg, a CONSORT checklist, contain information that should be better reported in the manuscript, or raise questions about the work? The STROBE checklist is completed, but a number of the items have not been adequately addressed as outlined in comments above and below</p>
RESULTS & CONCLUSIONS	<p>Are they credible? There appears to be some inaccuracy or unclear reporting. The average fall frequency index on lines 1-4, page 9 is reported to</p>

	<p>range from 1.63 (peripheral neuropathy) to 1.33 (dementia) referring to Figure 1. Figure 1, shows a range of 1 to approximately 1.63.</p> <p>Are they well presented?</p> <p>Be consistent in reporting results eg, in the paragraph commencing on line 24, page 8, report Chi2 result for each analysis.</p> <p>It is not clear how the categorical place of residence data was analysed?</p> <p>It seems appropriate to categorise fall frequency, however, these data would be more appropriately reported as number (%) in each category, rather than to present as a mean (error). Also, the fall frequency data is not comparable between neurological conditions, since of the wide range of sample sizes (from 7 to 58). It is not clear what variable the error bars refer to in figure 1.</p> <p>It is not clear what definition is being used for repeated falls (line 56, page 8) or multiple falls (Table2). Category 1 of the fall frequency index includes repeated fallers (ie, those who fell twice in the prior twelve months) as well as single fallers.</p> <p>Please include the disability, depression and balance confidence scores to give a clearer idea of the characteristics of the participants.</p> <p>Page 9, line 41 – these variables have been identified as risk factors, they are not necessarily predictive as prediction would need to be tested using area under the receiver-operating characteristic curve. “predictive” could be changed to “identified as risk factors”</p> <p>The percentages reported as “frequency of falls” (paragraph commencing line 10, page 9) appear to be “proportion of fallers”, ie, the percentage of individuals who fell in each category.</p> <p>Figure 3: The variables represented in these box and whisker plots need to be identified in the legend.</p> <p>Are the interpretation and conclusions warranted by and sufficiently derived from/focused on the data?</p> <p>The dementia, epilepsy, and headache groups are small n, and can be heavily influenced by outliers in analysis. The discussion of these results needs to be softened, eg, “New and quite astonishing” could read as “An unexpected result” “.....which needs to be interpreted with caution due to small sample size”. This issue also needs to be addressed under limitations.</p> <p>Are they discussed in the light of previous evidence?</p> <p>It seems inappropriate to refer to Oliver (ref 46) to support the suggestion for implementation of fall prevention programs in people with neurological conditions living in the community. Although there is good evidence for group and home-based exercise programs and home-safety interventions for prevention of falls in the elderly living in the community (Gillespie LD, 2012, Cochrane Database of Systematic Reviews 9;CD007146), there is less clear evidence for patients following stroke(eg, Verheyden G, 2013, Cochrane Database of Systematic Reviews 10; CD008728) and with PD (eg, Goodwin VA, 2011, JNNP 82:1232-38, Li F, 2012, NEJM 366(6)511-9).</p>
GENERAL COMMENTS	<p>To provide further insight into the generalisability of the findings, please indicate how many patients were initially screened, ie, prior to recruitment and neurological examination? The large drop out rate (23%) from neurological assessment to interview (for the neurological patients) should be acknowledged in the limitations section.</p> <p>The concluding sentence commencing line 29, page 10 needed to be toned down. Most elderly people have a number of co-morbidities. How they are screened for inclusion in research depends on the question being asked.</p>

	Under limitations, page 12, it would be better to simply acknowledge the limitations of retrospective falls data based on recall and to recommend that future prospective studies following established guidelines for reporting falls be conducted (Lamb SE, 2005, JAGS 53:1618-22)
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VERSION 1 – AUTHOR RESPONSE

Reactions to Reviewer 1 (Z Pirtosek):

As pointed out correctly by the reviewer, these findings do not only affect just neurologists but also a host of other professions and lay people involved with the care of neurological patients we replaced the word "neurologist" by a listing of other stake holders (last para of the conclusion section):

“General practitioners, geriatricians, neurologists and carers should therefore be aware that neurological patients are at high risk for falls, ...”

Reactions to Reviewer 2 (PW Overstall):

Consensus guidelines recommend the use of prospective falls diaries in studies on fall rates, eg monthly diaries returned to the researcher who can telephone patients to remind them if necessary. The absence of diaries is a serious flaw and means the fall rates are likely to be underestimated.

In the limitations section first para we added:

“... the problem that the number of falls is underreported.. ... remembering these events might pose a problem Future prospective studies could minimize this problem by using patients diaries according to established guidelines for reporting falls 46 possibly even in combination with wearable miniaturized electronic devices apt to objectively detect and monitor falls 47.”

And in the conclusion section:

“These [future] studies should also include more objective monitoring systems and ...”

Also it is not stated whether patients were given a simple definition of a fall and again this is necessary to ensure accuracy. For instance, was a fall during an epileptic fit counted as a fall?

The following definition of falls was applied and to clarify this we introduced the following sentence in the participants and methods section (subheading statistical analysis):

“Falls were defined according to the WHO definition 1 as an event which results in a person coming to rest inadvertently on the ground or floor or other lower level irrespective of cause, thus including e.g. falls from epileptic seizures.”

I imagine that many of these patients would have a fear of falling and this would be an interesting area to include if you are planning further studies. The effect of medication on balance in this group of patients would also be worth looking at. I entirely agree with your message that neurological patients should be regarded as having a high falls risk. Well done!

In response to this helpful suggestion we made the following final statement in the conclusion section:

“These [future] studies should also include more objective monitoring systems and include further potential risk factors like medication and fear of falling.”

Response to Reviewer 33 (Colleen G Canning)

1) Title

Suggest remove “various” from the title

“Various” was removed accordingly

2) Is the research question clearly defined?

a) Yes, however, there is already a substantial amount known about increased risk of falls in the stroke and Parkinson’s disease population and it is recommended that this be acknowledged (eg, Verheyden G, 2013, Cochrane Database of Systematic Reviews 10; CD008728; Allen NE, 2013, Parkinson’s disease 2013:906274).

p4 last para

“There is, however, substantially less known about the risk for falls in patients afflicted with various common neurological diseases. While there is already a substantial amount known about increased risk of falls in the stroke 10, Parkinson’s disease 11 or dementia 12 population, but to our knowledge there is only one comparative study investigating ed falls in patients with different a broad range of neurological diseases“

b) The potential new information relates to the cumulative effect of more than one neurological condition (and other conditions) and the risk of falls in yet unstudied populations, eg, such as headache.

In the section key messages we included the following:

- “The impact differs according to disease but those with impairments of the sensorimotor system are particularly endangered. However our findings investigating yet unstudied populations, eg, such as headache revealed that even neurological disorders not directly connected with gait and balance carry an unexpected high risk for falls and that there is a cumulative effect of more than one neurological condition on the risk of falls.”

3) Is the overall study design appropriate and adequate to answer the research question?

a) As a preliminary investigation, yes. Future studies using gold standard prospective falls monitoring are required

b) with larger sample sizes for neurological subgroups are required in order to confirm observations

In discussion we added:

P14 para last

“Therefore further larger scale multicenter neuro-geriatric surveys with larger sample sizes for neurological subgroups should be performed not only to confirm our observations but to acquire more extensive knowledge of the effectiveness of preventive measures in patient cohorts with various neurological conditions and different degrees of disability. These studies should also include more objective monitoring systems and include further potential risk factors like medication and fear of falling.”

(in red: reactions to Reviewer 2 and in blue: reactions to Reviewer 3)

And in the limitations section we added:

“Future prospective studies could minimize this problem by using patients diaries according to established guidelines for reporting falls 46 possibly even in combination with wearable miniaturized electronic devices apt to objectively detect and monitor falls 47.”

4) Are the participants adequately described, their conditions defined, and the inclusion and exclusion criteria described?

Inclusion and exclusion criteria are not clearly described. A small number of participants were included with dementia.

a) What specific criteria were used to exclude on the basis of cognitive impairment?

As previous studies had shown that reliable answers in interview situations can be expected from patients with a MMSE of 13 and more (Clark 2008), we excluded patients below this cut-off level. Patients were however not screened for cognitive impairment but rather when they provided symptoms indicative of dementia on history taking or showed signs thereof during base line examination then a MMSE was performed.

Thus in Selection of participants and baseline examination we included

“Cognitive impairment to an extent that an interview would no longer yield reliable results (MMSE≤12), was also a cause for exclusion.”

b) The control participants were required to be without other disabling medical conditions – could the

authors please provide examples of conditions that were in this category.

“They were recruited among friends and acquaintances of the author and his co-workers who were aged 60+ and without any history of neurological disorders or other disabling medical conditions like heart failure, chronic obstructive pulmonary disease or rheumatoid arthritis severe enough to cause limitation of ordinary physical activity”.

c) It is not clear that other disabling medical conditions were also excluded in those with neurological conditions?

Yes, disabling medical conditions were excluded in that, not ambulatory patients caused by all sorts of impairment or disability (neurological or other medical disease) were excluded from the study.

“Severely disabled patients who were no longer able to walk unaided or were in poor general condition, be it for reasons of neurological or other medical disease, were excluded from the study. Cognitive impairment to an extent that an interview would no longer yield reliable results (MMSE≤12), was also a cause for exclusion.”

d) It is not clear if the control participants were screened for cognitive impairment?

Controls were not routinely screened for cognitive impairment but rather when they had difficulties in mentally understanding our instructions or in answering our questions then they were offered a full neuropsychiatric workup in our memory clinic. If the person declined the offer then their data was not used for the study. A known diagnosis of even mild dementia or of MCI precluded the invitation to participate.

“Although not routinely screened for cognitive deficits, obvious signs of or a known diagnosis of dementia or even of mild cognitive impairment was a reason for exclusion.”

5) Are the patients representative of actual patients the evidence might affect?

It is not clear how many participants were invited to participate at the time of the neurological examination, how many declined and for what reasons. The Barthel index data presented in Table 2 suggests that those included were a relatively high-functioning group.

Results second para: the following sentence was included:

“Prior to recruitment, twenty patients were excluded because of inability to walk unaided and one due to severe dementia. Of those that met inclusion criteria five rejected enrolment and six other patients could not be enrolled due to inadequate language skills (n=1), severe aphasia (n=1), or severe presbycusis (n=4).”

6) Are the methods adequately described?

a) The paragraph titled “Epidemiological and environmental bases” could contain less detail.

(reduced from 150 to 42 words)

Heading was changed to “Setting”

“Data were collected at the general outpatient department of the Department of Neurology of the University Hospital in Graz, Austria. As visits to the outpatient department do not require specialist referrals, the disease spectrum largely resembles that seen by community based neurologists.”

b) Please explain how the 13 categories of neurological conditions were determined? For example, is this a standard classification reported in the literature?

The 13 categories derived from the fact that other than those 13 disease classes no disease in our cohort of consecutive patients reached a prevalence of more than 7 which we considered the absolute minimum for meaningful statistical analyses.

“Further calculations were done for subsamples of 13 neurological disorders with the highest prevalence ($n \geq 7$). The diagnoses were based on the ICD-10 system for classification of diseases.”

Disease 2013 ICD-10-CM Index 2013 ICD-10-CM code

PNP Hereditary and idiopathic neuropathy, Inflammatory polyneuropathy, Other and unspecified polyneuropathies G60, G61, G62

Parkinson D Parkinson's disease, Secondary parkinsonism G20-G21

P. Nerve Les. Mononeuropathies of upper and lower limb G56- G57

Stroke Cerebral infarction I63

Vertebral Pain Dorsalgia M54

Dementia Dementia F00-F03

other vasc. D Other cerebrovascular diseases I67

Epilepsy Epilepsy and recurrent seizures G40

Vertigo Disorders of vestibular function, Dizziness and giddiness H81, R42

other MD Other extrapyramidal and movement disorders G25

Tinnitus Tinnitus H93.-

Headache migraine and other headache syndromes G43-G44

Visual Disturb. Visual disturbances and blindness

H53-H54

c) It is not clear which measures were taken at the baseline assessment performed by CNH and which measures were collected in the telephone questionnaire? For example, the motor examination of the UPDRS and the Hoehn & Yahr scale requires observation by the examiner, but it appears these data were collected in the telephone interview? Also, these data don't appear to be reported in the results.

The full UPDRS including the UPDRS-ME and the Hoehn & Yahr scale were performed at baseline, but these data were not used for analyses and thus are not reported in the results. To avoid confusion we clarified this part in the method section.

During the telephone interview we did the UPDRS II and Schwab and England Scale which are questionnaire based and don't require face to face observation. As Reviewer 2 has correctly mentioned, the Schwab and England Scale score was (unintentionally) omitted, and thus is now

shown in the corrected paragraph of the result section:

“Higher disability scores in Parkinson patients expressed by higher UPDRS II (activities of daily living) (Γ -B=-0.238; $p=0.062$) and Schwab & England scores (Γ -B=-0.235; $p=0.070$) resulted in a trend toward more frequent falls.”

To avoid confusion we clarified this part in the participants and methods section:

“Parkinson patients were also rated according to the Schwab and England Scale and Part II of the Unified Parkinson’s Disease Rating Scale (UPDRS) 15.”

In the telephone interview we collected oral consent, and applied the questionnaire.

“...only subjects who had given verbal informed consent at the start of the telephone contact were interviewed.”

d) The ABC-6 scale does not appear to have administered according to the guidelines. In these guidelines participants are asked to “indicate your level of confidence in doing the activity without loss of balance or being unsteady”? (Powell and Meyers, Journals of Gerontology 1995;50A:M28-M34) which is different to being asked about confidence in doing the activity without falling.

The instruction were given to the patients according to the original guidelines. Thus, as you have pointed out correctly, it should read instead of “Participants judged their confidence not to fall during specific activities”:

“Participants judged their level of confidence in performing specific activities without loss of balance or being unsteady”

e) A more appropriate heading for this section would be simply “Balance Confidence”. I would also suggest that “analysis of” be removed from the other headings in this section.

According to the suggestion we changed the heading for this paragraph to “Balance Confidence” and removed “analysis of” from the other headings in this section.

f) Please provide the “predefined algorithm” mentioned on line 42, page 7.

The predefined algorithm consisted of the following process:

“For the matching process we used alphabetical lists of names of male and female neurological patients and likewise of healthy controls, sorted by age. Then working down the list we searched manually to find for each neurological patient one control subject of the same age. If no match was found then we looked for a control that was one year younger, then one year older, then two years and finally three years younger respectively older. “

This new para was included in the methods section

g) The rationale for identifying “matched pairs” of participants with a neurological condition and control is not clear, especially given that other than results presented in Table 1, all statistical analyses relate

to the larger cohorts (228 neurological outpatients and 193 healthy controls).

The rationale behind the statistical analyses was as follows:

As female gender and advanced age are considered confounding factors, we thought it important to compute the data comparing neurological patients and healthy controls by using the data of paired gender and age matched controls (this comprises all results found under the heading: Incidence of falls in neurological patients and healthy controls, on page 8; including those depicted in Table 1).

For the comparison of subgroups of neurological patients however there was no need to take the data from the cohort of patients that were matched to healthy controls and therefore here we used the larger cohort consisting of 228 neurological outpatients and 193 healthy controls. (these results are found under the heading: Risk factors for falls in neurological patients, on page 8)..

7) Is the main outcome measure clear?

a) Please state explicitly that the primary outcomes was falls, based on participant recall over the prior 12 months.

b) Please explain how a fall was defined and provide a reference for the definition?

We introduced the following sentence in the section Statistical analysis

“The primary outcomes was falls, based on participant recall over the prior 12 months. Falls were defined according to the WHO definition as an event which results in a person coming to rest inadvertently on the ground or floor or other lower level irrespective of cause, thus including e.g. falls from epileptic seizures. The one-year incidence of falls was calculated for both healthy elderly individuals and the whole sample of neurological patients.”

8) Are the abstract/summary/key messages/limitations accurate?

a) The abstract i)should state explicitly that falls data was based on 12 month recall of falls.

ABSTRACT

“Main outcome measures: One-year incidence of falls based on patients’ 12 month recall; motor and non- motor function tests to detect additional risk factors.”

ii) The percentages should be identified as proportion of fallers in each subgroup, not fall frequency.

“Results: 46% of patients and 16% of controls fell at least once a year. Patients with stroke (89%), Parkinson's disease (77%), dementia (60%) or epilepsy (57%) had a particularly high proportion of fallers, but even subgroups of patients with the least fall-associated neurological diseases like tinnitus (30%) and headache (28%) had a higher proportion of fallers than the control group.”

b) Article summary –

i)there is more than limited falls data on some neurological impairments, eg, PD and stroke, and

ii) most of this data relates to community dwelling persons

Article focus

Previous studies have shown that falls in the elderly are common and a substantial amount of data on single neurological conditions like stroke and Parkinson's disease suggest that neurological impairments further increase the risk for falls.

"However, little is known on the influence of a broad range of neurological diseases and how they differ among each other. No data is available on independent community dwelling senior citizens."

c) Key messages - The new information relates to the cumulative effect of more than one neurological condition (and other conditions) and the risk of falls in yet unstudied populations, eg, such as headache. This could be made clearer. Suggest remove "astonishingly"

According to this recommendation we adjusted the following:

"The results of our study suggest that all elderly neurological patients even when still ambulatory carry a heightened risk for falls.

□ The impact differs according to disease but those with impairments of the sensorimotor system are particularly endangered. However our findings investigating yet unstudied populations, eg, such as headache, revealed that even neurological disorders not directly connected with gait and balance carry an astonishingly unexpected high risk for falls and that there is a cumulative effect of more than one neurological condition on the risk of falls."

d) Strengths and limitations – although the design is prospective, the falls history is retrospective, based on recall over 12 mths.

"The following limitations should be considered: although the design is prospective, the falls history is retrospective, based on patients' recall over 12 months, therefore underreporting of cases is possible. Small sample sizes in some of the subgroups of neurological diseases. Participants were mostly of Caucasian origin and a quarter of patients was lost for follow up, which may limit the generalisability of the results to other populations."

9) Are the statistical methods described?

10) Are they appropriate?

It is reported that risk odds ratios were computed – please clarify whether these are odds ratios or risk ratios? The results should be amended in line with this.

We omitted the word risk as it was odds-ratios that were computed

Thus the text in Statistical analysis was changed to:

"For the identification of fall related risk factors, correlations (Kendall's τ -B), and for the individual neurological disorders, risk odds ratios were computed (α -level of significance $p < 0.05$)."

11) Is the standard of written English acceptable for publication?

English language editing would improve clarity

12) Are references up to date and relevant?

Ref 2 – this Cochrane review was updated in 2012 (Gillespie LD, 2012, Cochrane Database of Systematic Reviews 9;CD007146)

This Reference was replaced by the updated Cochrane review

Ref 11 – this is a retrospective study of falls in people with PD. There are several high quality prospective studies, which would be more appropriately referenced, eg, Latt MD, 2009, Movement Disorders 24:1280-9; Kerr GK, 2010, Neurology 75:116-24; Paul SS, 2013, Movement Disorders 28:655-62.

See also comments relating to discussion

This Reference was replaced by Paul et al., Three Simple Clinical Tests Movement Disorders 2013, 28:655-62.

Do any supplemental documents, eg, a CONSORT checklist, contain information that should be better reported in the manuscript, or raise questions about the work?

The STROBE checklist is completed, but a number of the items have not been adequately addressed as outlined in comments above and below

give page and line numbers

page and line numbers were added to STROBE checklist

Are they credible?

There appears to be some inaccuracy or unclear reporting. The average fall frequency index on lines 1-4, page 9 is reported to range from 1.63 (peripheral neuropathy) to 1.33 (dementia) referring to Figure 1. Figure 1, shows a range of 1 to approximately 1.63.

There is a range from 1 to 1.63 for all 13 diseases, whereas the range in the five diseases with the highest propensity for multiple falls is 1.33 -1.63

“Multiple falls occurred particularly in patients with peripheral neuropathy (43%), peripheral nerve lesion (43%), dementia (33%), Parkinson's disease (30%), stroke (30%) and vertebral pain (30%). The average fall frequency index in this group of five diseases ranged from 1.63 (peripheral neuropathy) to 1.33 (dementia).”

Are they well presented?

Be consistent in reporting results eg, in the paragraph commencing on line 24, page 8, report Chi2 result for each analysis.

Accordingly we added the the respective Chi2 results

“One hundred and six (46.5%) neurological patients but only 31 (16.1%) healthy controls had fallen at least once (Chi2=43.4; p <0.001) during this one-year period.”

It is not clear how the categorical place of residence data was analysed?

This was analysed computing correlation coefficients(Kendall's Tau) for nonparametric variables.

“For healthy controls, however, their place of residence had an influence, in that subjects living in more rural environments were more prone to falls (Γ -B=0.217; $p<0.001$).”

It seems appropriate to categorise fall frequency, however, these data would be more appropriately reported as number (%) in each category, rather than to present as a mean (error). Also, the fall frequency data is not comparable between neurological conditions, since of the wide range of sample sizes (from 7 to 58). It is not clear what variable the error bars refer to in figure 1.

Fig 1 was according to these recommendations completely restructured and now depicts number (%) in each category.

It is not clear what definition is being used for repeated falls (line 56, page 8) or multiple falls (Table2). Category 1 of the fall frequency index includes repeated fallers (ie, those who fell twice in the prior twelve months) as well as single fallers.

This is indeed misleading. Repeated falls should rather be exchanged with the term multiple falls.

“Multiple falls occurred particularly in patients with peripheral neuropathy (43%), peripheral nerve lesion (43%), dementia (33%), Parkinson's disease (30%), stroke (30%) and vertebral pain (30%).

Likewise we included the definition of multiple falls at the legend of table 2:

“Multiple falls were defined as more then two falls per year (i.e. a Fall Frequency Index ≥ 2)”

Please include the disability, depression and balance confidence scores to give a clearer idea of the characteristics of the participants.

According to the suggestion, disability, depression and balance confidence scores were included in Table 1

Page 9, line 41 – these variables have been identified as risk factors, they are not necessarily predictive as prediction would need to be tested using area under the receiver-operating characteristic curve. “predictive” could be changed to “identified as risk factors”

“Severity of depression as reflected by a higher ADS score (Γ -B=0.329; $p<0.001$) and low balance confidence reflected by higher ABC scores (Γ -B=-0.384; $p<0.001$) were also identified as risk factors (Fig. 3).”

The percentages reported as “frequency of falls” (paragraph commencing line 10, page 9) appear to be “proportion of fallers”, ie, the percentage of individuals who fell in each category.

The type of neurological disease the patient was afflicted with influenced the proportion of fallers in that patients post stroke (89%), with Parkinson's disease (77%), dementia (60%) and epilepsy (57%) had the highest frequency of falls.

Figure 3: The variables represented in these box and whisker plots need to be identified in the legend.

“Fig.3a,b Differences in ABC-6 scores (3a) and number of neurological diseases (ND) (3b) of neurological patients with and without falls indicate that fallers as compared to non-fallers have lower

confidence in their balance and a higher number of concomitant neurological diseases.
(ABC-6% meaning percentage scores of the 6-item version of the Activities-Specific Balance Confidence scale, number of ND meaning number of neurological diseases a patient is afflicted with)"

Are the interpretation and conclusions warranted by and sufficiently derived from/focused on the data?

The dementia, epilepsy, and headache groups are small n, and can be heavily influenced by outliers in analysis. The discussion of these results needs to be softened, eg, "New and quite astonishing" could read as "An unexpected result" ".....which needs to be interpreted with caution due to small sample size". This issue also needs to be addressed under limitations.

We proceeded accordingly and made the following changes:
Page 11) (discussion)

"An unexpected result was that even patients suffering from neurological diseases with no direct influence on gait or balance like headache (28%) had almost twice as many falls as the average healthy control (16,1%). However this needs to be interpreted with caution due to small sample size."

Page 13) (limitations)

"Others, particularly the dementia group with only seven patients, is, due to the exclusion of the more affected, quite small and allows only limited extrapolation. The same holds true for epilepsy and headache. Nevertheless, it is remarkable that even here the analysis of difference reached levels of significance."

Are they discussed in the light of previous evidence?

Page 14 (conclusion)

"For patients with several of these factors, targeted prevention programs might be beneficial.⁴⁶ However, also they have been shown to generally reduce falls and injuries in the community dwelling elderly there is but inconclusive evidence for patients following stroke (Verheyden 2013) and with PD (Goodwin 2011, Li 2012) and even more scanty information for patients with other neurological diseases.. Therefore, further larger scale multicenter neuro-geriatric surveys with larger sample sizes for neurological subgroups should be performed not only to confirm our observations but to acquire more extensive knowledge of the effectiveness of preventive measures in patient cohorts with various neurological conditions and different degrees of disability. These studies should also include more objective monitoring systems and include further potential risk factors like medication and fear of falling."

Is the article reported in line with the appropriate reporting statement or checklist.

The STROBE checklist is completed, but a number of the items have not been adequately addressed as outlined in comments above. It is useful to indicate the page of the manuscript on which each of the items is addressed.

Are research ethics (eg, consent, ethical approval) addressed appropriately?

It is stated that the survey, including all details concerning the selection process, was approved by the Ethics Committee of the Medical University Graz.

It is also stated that only subjects who had given informed consent beforehand were interviewed. Please clarify whether informed consent was written or verbal and when it was obtained?

The consent was verbal and at the time of the interview. A special consent form that was read to the participant aloud was reserved for this, including the documentation of the positive or negative reaction of the participant and the mandatory signature of the interviewer.

“A telephone follow-up was scheduled 12 months after the baseline outpatient visit; it was carried out by one of two examiners (AP, MG) following a predefined format and only subjects who had given verbal informed consent at the start of the telephone contact were interviewed.”

To provide further insight into the generalisability of the findings, please indicate how many patients were initially screened, ie, prior to recruitment and neurological examination? The large drop out rate (23%) from neurological assessment to interview (for the neurological patients) should be acknowledged in the limitations section.

Accordingly the following paragraph was introduced:

“Twenty patients were excluded prior to recruitment because of inability to walk unaided and one due to severe cognitive impairment. Six other patients that met inclusion criteria could not be enrolled because of inability to participate due to inadequate proficiency of the German language (n=1), severe aphasia (n=1), or severe presbycusis (n=1), and five patients rejected participation. “

Page 12)

“Secondly, the large drop out rate of 23 from neurological assessment to interview, not containing the 3,6% that had to be excluded prior to recruitment due to inability or unwillingness to participate could have lead to further underestimating the number of patients with falls.”

The concluding sentence commencing line 29, page 10 needed to be toned down. Most elderly people have a number of co-morbidities. How they are screened for inclusion in research depends on the question being asked.

This shows that it can be of advantage, when studying groups of elderly patients, to have a truly healthy control group, as in our survey.

Under limitations, page 12, it would be better to simply acknowledge the limitations of retrospective falls data based on recall and to recommend that future prospective studies following established guidelines for reporting falls be conducted (Lamb SE, 2005, JAGS 53:1618-22)

“The risk for falls in neurological patients might therefore be greater than shown in any results. Future prospective studies could minimize this problem by using patients diaries according to established guidelines for reporting falls (Lamb SE, 2005, JAGS 53:1618-22) possibly in combination with wearable miniaturized electronic devices apt to objectively detect and monitor falls (Howcroft 2013)”.

VERSION 2 – REVIEW

REVIEWER	Colleen Canning University of Sydney, Australia
REVIEW RETURNED	22-Oct-2013

GENERAL COMMENTS	The authors have addressed the major issues raised by reviewers. I
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	<p>have a few additional/editorial comments which I hope will assist to further improve the clarity of the paper. In addition, clarity would be further enhanced if an English language editorial review was undertaken.</p> <p>Additional comments: Since the conclusion has been amended to refer to "General practitioners, geriatricians, neurologists and carers....", please consider including other health professionals who manage patients at risk of falls , such as physiotherpists. This sentence could be amended more broadly to read "Medical practitioners, allied health professionals and carers...." The wording in the abstract should be consistent with the conclusion in this respect.</p> <p>page 8, line 38 - "Out of 126 neurological patients experiencing falls" should read "Out of 106 neurological patients experiencing falls", ie, it should be consistent with the result on page 8, line 36.</p> <p>page 8, line 43 - "Out of 76 individuals with a history of falls" should read "Out of 31 individuals with a history of falls" ie, it should be consistent with the result on page 8, line 36.</p> <p>page 9, line 55 - Low balance confidence is reflected by lower ABC scores, not higher ABC scores</p> <p>page 11, line 5 - The inverse U relationship between falls and progressive immobility has been proposed previously by Bloem with respect to Parkinson's disease and warrants acknowledgement. Bloem BR (2001) Postural instability and falls in Parkinson's disease. Advances in Neurology 87:209-223.</p> <p>Page 11, line 55 - "repetitive falls". Please be consistent with terminology throughout the paper. Based on the authors definitions, I think this should read "multiple falls". Similarly, on Page 11, line 59, reconsider the use of the word "recurrent". Should this be "repeated" or "multiple"?</p> <p>Page 11, line 60 - suggest replace "quite astonishing" with "unexpected" (as this replacement has been made elsewhere in the paper)</p> <p>Page 12, line 57 - suggest reword to "the number of falls are likely to be underreported"</p> <p>Figure 1 - is not just percentage of multiple fallers, it includes those who fell once or twice.</p>
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VERSION 2 – AUTHOR RESPONSE

Changed in abstract and conclusion to "Medical practitioners, allied health professionals and carers"

page 8, line 38 - "Out of 126 neurological patients experiencing falls" should read "Out of 106 neurological patients experiencing falls", ie, it should be consistent with the result on page 8, line 36.

"126" changed to "106"

page 8, line 43 - "Out of 76 individuals with a history of falls" should read "Out of 31 individuals with a history of falls" ie, it should be consistent with the result on page 8, line 36.

"76" changed to "31"

page 9, line 55 - Low balance confidence is reflected by lower ABC scores, not higher ABC scores

"higher ABC scores" changed "lower ABC scores"

page 11, line 5 - The inverse U relationship between falls and progressive immobility has been proposed previously by Bloem with respect to Parkinson's disease and warrants acknowledgement. Bloem BR (2001) Postural instability and falls in Parkinson's disease. *Advances in Neurology* 87:209-223.

"Since this concept is not yet backed up by sound evidence, further studies directly comparing the risk of falling in neurological inpatients and outpatients of various grades of disability are needed to support this assumption."

Changed to:

"Since this concept has yet only been proposed for PD (Bloem 2001) but not for other neurological conditions, further studies directly comparing the risk of falling in neurological inpatients and outpatients of various grades of disability are needed to support this assumption."

Page 11, line 55 - "repetitive falls". Please be consistent with terminology throughout the paper. Based on the authors definitions, I think this should read "multiple falls". Similarly, on Page 11, line 59, reconsider the use of the word "recurrent". Should this be "repeated" or "multiple"?

"Confirmative data also obtained from small cohorts revealed that repetitive falls occurred in 10 out of 25 (40%) neuropathy patients 42 and another 13 out of 20 neuropathy patients (65%) had a propensity for recurrent falls for an average of 5.8 falls per year 40."

Was changed to:

"Confirmative data also obtained from small cohorts revealed that multiple falls occurred in 10 out of 25 (40%) neuropathy patients 42 and another 13 out of 20 neuropathy patients (65%) had a propensity for multiple falls for an average of 5.8 falls per year 40."

Page 11, line 60 - suggest replace "quite astonishing" with "unexpected" (as this replacement has been made elsewhere in the paper)

"New and quite astonishing was the fact that ..."

Was changed to:

"New and unexpected was the fact that ..."

Page 12, line 57 - suggest reword to "the number of falls are likely to be underreported"

“... the problem that the number of falls is underreported.”

Was changed to:

“... the problem that the number of falls are likely to be underreported.”

Figure 1 - is not just percentage of multiple fallers, it includes those who fell once or twice.

The term of “multifallers” was replaced with “fallers”